

5 I Claim:

1. A method for treating a condition of the central nervous system selected from one of the following: seizures; seizure disorders; epilepsy; status epilepticus; migraine headache; cortical spreading depression; headache; intracranial hypertension; central nervous system edema; neuropsychiatric disorders; neurotoxicity; head trauma; stroke; ischemia and hypoxia in a mammalian subject comprising administering an effective amount of a treatment composition having ion-dependent cotransporter antagonist activity to the mammalian subject.

2. A method of claim 1, wherein the treatment composition has cation-chloride cotransporter antagonist activity.

3. A method of claim 1, wherein the treatment composition has higher activity as a glial cell cation-chloride cotransporter antagonist than as a neuronal cell cation-chloride dependent cotransporter antagonist.

4. A method of claim 1, wherein the treatment composition has higher activity as a glial cell cation-chloride cotransporter antagonist than as a renal cell cation-chloride cotransporter antagonist.

5. A method of claim 1, wherein the treatment composition is selected from the group consisting of: loop diuretics and loop diuretic-like compositions, furosemide and furosemide-like compositions, thiazides and thiazide-like compositions.

6. A method of claim 1, wherein the treatment composition comprises a first composition selected from the group consisting of: loop diuretics and loop diuretic-like compositions, furosemide and furosemide-like compositions, thiazides and thiazide-like compositions, bendoflumethiazide, benzthiazide, chlorothiazide; hydrochlorothiazide, hydroflumethiazide, methclothiazide, polythiazide, trichlormethiazide, chlorthalidone, indapamide, metolazone and quinethazone; and a second composition selected from the group consisting of: phenytoin, carbamazepine, barbiturates, Phenobarbital, pentobarbital, mephobarbital, trimethadione, mephentyoin, paramethadione, phenthenylate, phenacemide, metharbital, benzchlorpropanmide, phensuximide,

5 primidone, methsuximide, ethosuximide, valporate, felbamate, gabapentin, lamotrigine,  
 clorazepate, fosphenytoin, ethosuximide, valporate, felbamate, gabapentin, lamotrigine,  
 topiramate, vigabatrin, tiagabine, zonisamide, clobazam, thiopental, midazolam,  
 propofol, levetiracetam, oxcarbazepine, CCPene, GYK152466, sumatriptan, non-steroidal  
 anti-inflammatory drugs, neuroleptics, corticosteroids, vasoconstrictors, beta-blockers,  
 10 antidepressants, anticonvulsants, particularly Depakote, Ergot alkaloids, tryptans,  
 Acetaminophen, caffeine, Ibuprofen, Propoxyphene, oxycodone, codeine,  
 isometheptene, serotonin receptor agonists, ergotamine, dihydroergotamine, sumatriptan,  
 propranolol, metoprolol, atenolol, timolol, nadolol, nifedipine, nimodipine, verapamil,  
 aspirin, ketoprofen, tofenamic acid, mefenamic acid, naproxen, methysergide,  
 15 paracetamol, clonidine, lisuride, ipرازochrome, butalbital, benzodiazepines, and  
 divalproex sodium.

7. A method of claim 1, wherein the subject is a human.

20 8. A method of claim 1, additionally comprising administering an effective  
 amount of a blood brain barrier permeability enhancer.

9. A method of claim 1, additionally comprising administering a  
 hyperosmotic agent.

25 10. A method for treating a condition of the central nervous system selected  
 from one of the following: seizures; seizure disorders; epilepsy; status epilepticus;  
 migraine headache; cortical spreading depression; headache; intracranial hypertension;  
 central nervous system edema; neuropsychiatric disorders; neurotoxicity; head trauma;  
 30 stroke; ischemia and hypoxia in a mammalian subject comprising administering an  
 effective amount of a treatment composition that modulates the synchronization of  
 neuronal discharges in the central nervous system (CNS).

35 11. A method of claim 10, wherein the treatment composition produces  
 diminished hypersynchronization of neuronal population activity in the CNS.

5 12. A method of claim 10, wherein the treatment composition produces modulation of the chloride concentration in extracellular space in the CNS.

13. A method for treating migraine headache, cortical spreading depression and other headache conditions in a mammalian subject comprising administering an  
10 effective amount of a treatment composition having cation-chloride cotransporter antagonist activity to the mammalian subject.

14 A method of claim 13, comprising administering an agent selected from the group consisting of: loop diuretics and loop diuretic-like compositions, furosemide  
15 and furosemide-like compositions, thiazides and thiazide-like compositions, bendoflumethiazide, benzthiazide, chlorothiazide; hydrochlorothiazide, hydroflumethiazide, methclothiazide, polythiazide, trichlormethiazide, chlorthalidone, indapamide, metolazone and quinethazone.

20 15. A method of claim 14, additionally comprising administering an agent selected from the group consisting of: non-steroidal anti-inflammatory drugs, neuroleptics, corticosteroids, vasoconstrictors, beta-blockers, antidepressants, anticonvulsants, particularly Depakote, Ergot alkaloids, tryptans, Acetaminophen, caffeine, Ibuprofen, Propoxyphene, oxycodone, codeine, isometheptene, serotonin  
25 receptor agonists, ergotamine, dihydroergotamine, sumatriptan, propranolol, metoprolol, atenolol, timolol, nadolol, nifedipine, nimodipine, verapamil, aspirin, ketoprofen, tofenamic acid, mefenamic acid, naproxen, methysergide, paracetamol, clonidine, lisuride, ipرازochrome, butalbital, benzodiazepines, and divalproex sodium.

30 16. A treatment agent comprising a composition having cation-chloride cotransporter antagonist activity, and having higher activity as a glial cell cation-chloride cotransporter antagonist than as a neuronal cell ion-dependent cotransporter antagonist.

35 17. A treatment agent of claim 23, wherein the composition additionally has higher activity as a glial cell cation-chloride cotransporter antagonist than as a renal cell cation-chloride cotransporter antagonist.

5           18.     A treatment agent comprising a combination of a first composition having  
ion-dependent cotransporter antagonist activity and a second composition selected from  
the group consisting of: phenytoin, carbamazepine, barbiturates, Phenobarbital,  
pentobarbital, mephobarbital, trimethadione, mephentyoin, paramethadione,  
phenthenylate, phenacemide, metharbital, benzchlorpropanmide, phensuximide,  
10    primidone, methsuximide, ethotoin, aminoglutethimide, diazepam, clonazepam,  
clorazepate, fosphenytoin, ethosuximide, valporate, felbamate, gabapentin, lamotrigine,  
topiramate, vigabatrin, tiagabine, zonisamide, clobazam, thiopental, midazolam,  
propofol, levetiracetam, oxcarbazepine, CCPene, GYK152466, sumatriptan, non-steroidal  
anti-inflammatory drugs, neuroleptics, corticosteroids, vasoconstrictors, beta-blockers,  
15    antidepressants, anticonvulsants, particularly Depakote, Ergot alkaloids, tryptans,  
Acetaminophen, caffeine, Ibuprofen, Propoxyphene, oxycodone, codeine,  
isometheptene, serotonin receptor agonists, ergotamine, dihydroergotamine, sumatriptan,  
propranolol, metoprolol, atenolol, timolol, nadolol, nifedipine, nimodipine, verapamil,  
aspirin, ketoprofen, tofenamic acid, mefenamic acid, naproxen, methysergide,  
20    paracetamol, clonidine, lisuride, iprazochrome, butalbital, benzodiazepines, and  
divalproex sodium.

          19.     A treatment agent of claim 18, wherein the first composition is selected  
from the group consisting of: loop diuretics and loop diuretic-like compositions,  
25    furosemide and furosemide-like compositions, thiazides and thiazide-like compositions,  
bendoflumethiazide, benzthiazide, chlorothiazide; hydrochlorothiazide,  
hydroflumethiazide, methclothiazide, polythiazide, trichlormethiazide, chlorthalidone,  
indapamide, metolazone and quinethazone.

30           20.     A treatment agent of claim 18, additionally comprising a blood brain  
barrier permeability enhancer.